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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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10/500,690

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Mark Pines

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ROPES & GRAY LLP
PATENT DOCKETING 39/361
1211 AVENUE OF THE AMERICAS
NEW YORK, NY 10036-8704

EXAMINER

BALASUBRAMANIAN, VENKATARAMAN

ART UNIT

PAPER NUMBER

1624

MAIL DATE

DELIVERY MODE

11/13/2008

PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No. 10/500,690	Applicant(s) PINES ET AL.	
	Examiner /Venkataraman Balasubramanian/	Art Unit 1624	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 23 July 2008.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-14 and 24-30 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-14 and 24-30 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Applicants' response, which included cancellation of claims 15-23, addition of new claim 30 and amendment to claims 1, 7-9, 11, 13, 14, 24, 27 and 28, filed on 7/23/2008, is made of record. Claims 1-14 and 24-30 are pending.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 11, 14 and 28 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

1. Claim 11 is indefinite as it recites a "solvent" thereof. It is not clear what is intended.
2. Claims 11, 14 and 28 are improper dependent claims as they fail to further limit claim 1 on which they are dependent and have scope broader than claim 1. Not claim 1 does not include "hydrate" while claims 11, 14 and 28 recite hydrate which is outside the scope of claim 1.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 1-14 and 24-30 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably

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convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Recitation of “wherein said quinazolinone compound and said at least one additional antitumor treatment are effective synergistically” in claim 1 introduces new matter. Specification has no support for such a synergistic effect. Specification clearly recites radiation and chemotherapy treatment of tumor results in fibrosis and such a fibrosis can be treated with quinazolinone. This is not synergistic antitumor effect. Therefore amendment to claim 1 has introduced new matter.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein

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were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-6, 8, 10-14, 24-28 and 30 are rejected under 35 U.S.C. 103(a) as being unpatentable over Pines et al., WO 98/34613 and in view of Nagler et al., Am. J. Respir. Crit. Care Med. 154(4 Pt 1): 1082-1086, 1996. PubMed Abstract provided.

Pines et al., teaches method of use of quinazolinone containing pharmaceutical compositions including halofuginone for treating various malignancies. See pages 1-13 details of the invention. Especially see page 6 for compound shown therein and page 12 for treating various cancers. See 15-16 for preferred embodiments and pages 17-38 for examples 1-17 teaching use of halofuginone for treating various tumors.

Instant claims recite use of halofuginone and compound of formula I in combination with chemotherapeutic agents.

Pines et al., do not explicitly recite use of such halofuginone or related compounds stated above for combination therapy. However, treatment of cancer is often done with combination therapy and hence one trained the art would be motivated to use halofuginone or its analogs taught by Pines et al., with other chemotherapeutic agents.

In addition, Nagler et al., clearly shows the beneficial effect of halofuginone in bleomycin induced pulmonary fibrosis. See entire PubMed abstract. Bleomycin is

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routinely used in treating cancer and this is evident from instant claim 12, which lists bleomycin as one of the chemotherapeutic agent.

Thus, it would be obvious to one trained in the art at the time of instant invention to use halofuginone in combination with chemotherapeutic agents to treat various cancers. See also *In re KSR International vs Teleflex Inc.*, 82 USPQ2d 13-85, 1397 (2007).

This rejection is same as made in the previous office action but limited those claims which recite use of chemotherapy. Applicants' argument to overcome this rejection is not persuasive.

First of all, bleomycin is a well known anticancer agent and is currently used for treating specific cancers. Various prior art , instant specification and instant claim 12 clearly lend support for this.

Secondly, bleomycin, besides other side effects, induces fibrosis. This clearly shown in the above cited reference Nagler et al., and other prior art. Instant specification also clearly acknowledges that this fact is known in the prior art. See pages 1-3, especially page 2 and 3.

Thirdly, Nagler et al., shows that fibrosis induced by bleomycin can be treated with halofuginone. It is also known in the prior art that halofuginone and its derivatives are useful for fibrotic condition (US 5,449,678) and instant specification clearly acknowledges this fact. See page 3 and 4.

Hence, one trained in the art would known that halofuginone and the related compounds disclosed in the primary reference would be useful for treating fibrosis in

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cancer patients who were treated with bleomycin. Hence, one trained in the would be motivated to use a combination therapy using anticancer agents that induce fibrosis with halofuginone and its derivatives based on the combined teaching of the primary and secondary references cited above.

Also see *KSR International Co. v. Teleflex Inc.*, 127 S.Ct. 1727 (2007), wherein the court stated that

[w]hen there is a design need or market pressure to solve a problem and there are a finite number of identified, predictable solutions, a person of ordinary skill has good reason to pursue the known options within his or her technical grasp. If this leads to the anticipated success, it is likely the product not of innovation but of ordinary skill and common sense.

Such is the case with instant claims. Hence, based on teachings and guidance provided in the combined prior art, one trained in the art would be motivated to halofuginone and its derivative in combination therapy with anticancer agents including bleomycin.

Hence, this rejection is proper and is maintained.

Conclusion

Any inquiry concerning this communication from the examiner should be addressed to Venkataraman Balasubramanian (Bala) whose telephone number is (571) 272-0662. The examiner can normally be reached on Monday through Thursday from 8.00 AM to 6.00 PM. The Supervisory Patent Examiner (SPE) of the art unit 1624 is James O. Wilson, whose telephone number is 571-272-0661. The fax phone number for

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the organization where this application or proceeding is assigned (571) 273-8300. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571) 272-1600.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAG. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-2 17-9197 (toll-free).

/Venkataraman Balasubramanian/

Primary Examiner, Art Unit 1624